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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/490,700	01/24/2000	Bernard Conrad	61130/JPW/KRD	7519

7590 11/21/2003

Ivor R. Elrifi
Mintz Levin
One Financial Center
Boston, MA 02111

EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/21/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/490,700

Applicant(s)

CONRAD ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 62-65, 73, 78 and 79 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 62, 73, 78 and 79 is/are allowed.
- 6) ☒ Claim(s) 63-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☒ Other: *Sequence alignment (2 pages)*.

DETAILED ACTION

Claims 63-65 have been amended. Claims 66-72 and 74-77 have been canceled.

Claims 62-65, 73, 78, and 79 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in view of applicant's amendment.

Claim 65 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 recites "wherein the amino acid sequence of the variant comprises a conservative substitution". It is unclear whether "a conservative substitution" refers to an isolated polypeptide comprising SEQ ID NO:35, having a single conservative substitution within the isolated polypeptide, or if "a conservative substitution" refers to a single amino acid substitution within SEQ ID NO:36. For purpose of examination, all alternatives will be considered. Further, it is noted that the recitation of a variant comprising a conservative substitution in addition to a non-conservative substitution or a deletion or truncation, or does not it exclude a variant comprising more than one conservative substitution.

Claims 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

Art Unit: 1642

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 64 is drawn to an isolated polypeptide comprising a variant of SEQ ID NO:36, having at least 95 % identity to SEQ ID NO:36, wherein the variant has superantigen activity. Claim 65 is drawn to an isolated polypeptide comprising a variant of SEQ ID NO:36 wherein the amino acid sequence of the variant comprises a conservative amino acid substitution and where the variant has superantigen activity. The specification contemplates variants having at least 80 % homology and at least 90 % homology to the proteins of the instant invention on page 26, lines 3-10. Neither the claims as originally filed, nor any other recitation within the specification provide support for the aforesaid limitations. One of skill in the art would reasonably conclude that applicant would not in possession of the claimed variants.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 63 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Ono et al, J Virol. 1986 Nov;60(2):589-98.

Claim 63 is drawn to a protein comprising amino acid sequences having at least 90 % identity to SEQ ID NO:36 with superantigen activity and claim 65 is more broadly

drawn to a variant of SEQ ID NO:36 comprising amino acid sequences with a conservative amino acid substitution, wherein said variant has superantigen activity.

Ono et al teach two human endogenous retrovirus genome HERV-K10 encoded polypeptides with 94.3 % and 91.5 % sequence identity respectively to instant SEQ ID NO:36, thus anticipating instant claim 63 in terms of sequence identity. Note the attached sequence alignment. As for the instant claim 65, the prior art sequences have "a conservative amino acid substitution" (note the pink-shaded area in the sequence alignment), thus anticipating the structural limitation of instant claim 65. Ono et al do not teach whether the proteins have superantigen activity. However, the instant specification at Fig. 6B and 6D suggests that the prior art sequences mostly likely have superantigen activity. Determining whether the sequences of the prior art possess the function requires experiments. However, the Office does not have facilities to perform such experiments, therefore cannot provide the factual evidence needed in order to establish that the two sequences of the prior art do not possess the superantigen activity. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed protein sequences are different from those taught by the prior art and to establish patentable differences.

All other rejections and objections as set forth in Paper No. 20 are withdrawn.

Allowable Subject Matter

Claims 62, 73, 78, and 79 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-

Art Unit: 1642

308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
November 16, 2003

Harun A. Gamble

SEQUENCE FROM N.A.
MEDLINE-9844962; PubMed-9778243;
RA Ian M.S., Mason A., Coutant R., Chen Q.Y., Vargas A., Rao J.,
RA Gomez R., Chalew S., Garry R., MacLaren N.K.,
RT "HERV-K10s and Immune-mediated (type 1) diabetes."
RL Cell 95:14-16(1998).
DR EMBL: AF084870; AAC68899.1;
KW Envelope protein.
SO SEQUENCE 153 AA; 17406 MW; 90B91BCE040C5A3 CRC64;

Query Match 95.8%; Score 805; DB 4; Length 153;
Best Local Similarity 96.7%; Pred. No. 7.2e-78;
Matches 148; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

QY 1 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 60
DB 1 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 60
QY 61 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 120
DB 61 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 120
QY 121 PKGSKNTEVLWMECVANSVILQNNNEFTIID 153
DB 121 PKGSKNTEVLWMECVANSVILQNNNEFTIID 153

RESULT 6
Q9HDB8 PRELIMINARY; PRT; 245 AA.
AC 09HDB8;
DT 01-MAR-2001 (TREMBlrel. 16, Created)
DT 01-MAR-2001 (TREMBlrel. 16, Last sequence update)
DT 01-MAR-2001 (TREMBlrel. 16, Last annotation update)
GN ENV.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.
OX NCBI_TaxID=9606;
RN 11
RP SEQUENCE FROM N.A.
RA Jimo Y., Sugimoto J.;
RT "Human endogenous retrovirus HERV-K(11) and flanking sequences."
RL Submitted (Aug-2000) to the EMBL/Genbank/DBD databases.
DR EMBL: AB047240; BAB11760.1;
SO SEQUENCE 245 AA; 27904 MW; 198F26D5ED56DDB CRC64;

Query Match 95.8%; Score 805; DB 4; Length 245;
Best Local Similarity 96.7%; Pred. No. 1.2e-77;
Matches 148; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

QY 1 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 60
DB 1 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 60
QY 61 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 120
DB 61 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 120
QY 121 PKGSKNTEVLWMECVANSVILQNNNEFTIID 153
DB 121 PKGSKNTEVLWMECVANSVILQNNNEFTIID 153

RESULT 7
Q14273 PRELIMINARY; PRT; 1361 AA.
AC 014273;
DT 01-NOV-1996 (TREMBlrel. 01, Created)
DT 01-NOV-1996 (TREMBlrel. 01, Last sequence update)

DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE POL/ENV ORF.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.
OX NCBI_TaxID=9606;
RN 11
RP SEQUENCE FROM N.A.
RA TISSUE=LIVER.
RX MEDLINE-87036922; PubMed-3021993;
RA Ono M., Yasunaga T., Miyata T., Ushikubo H.;
RT "Nucleotide sequence of human endogenous retrovirus genome related to
RT the mouse mammary tumor virus genome."
RL J. Virol. 60:589-598(1986).
CC -1- SIMILARITY: TO RNA-DIRECTED DNA POLYMERASE (REVERSE
CC TRANSCRIPTASE).
DR EMBL: M4123; AAA88033.1;
DR InterPro: IPR001037; Integrase_C.
DR InterPro: IPR003308; Integrase_Zn.
DR InterPro: IPR002156; RNaseH.
DR InterPro: IPR004777; RNase.
DR Pfam: PF00552; Integrase_1.
DR Pfam: PF02022; Integrase_Zn_1.
DR Pfam: PF00075; RNaseH_1.
DR Pfam: PF00665; Rve_1.
DR Pfam: PF00078; Rvt_1.
KW RNA-directed DNA polymerase.
SO SEQUENCE 1361 AA; 15379 MW; CEB91B3F407B9498 CRC64;

Query Match 94.3%; Score 792; DB 4; Length 1361;
Best Local Similarity 94.8%; Pred. No. 2.1e-75;
Matches 145; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

QY 1 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 60
DB 774 MVTPTWMDNPIEVYVNDVWVPGPTDRCAPAKPEEGMINISIGYHYPPICLGRAPGC 833
QY 61 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 120
DB 834 LMPAVQNMVLVEVPTVSPNSRFTYHMGSLRPVNYLDFSYORSLSKFRPKGKCPKEI 893
QY 121 PKGSKNTEVLWMECVANSVILQNNNEFTIID 153
DB 894 PKGSKNTEVLWMECVANSVILQNNNEFTIID 926

RESULT 8
Q9UKH9 PRELIMINARY; PRT; 2294 AA.
AC 09UKH9;
DT 01-MAY-2000 (TREMBlrel. 13, Created)
DT 01-MAY-2000 (TREMBlrel. 13, Last sequence update)
DT 01-JUN-2001 (TREMBlrel. 17, Last annotation update)
DE GAG-PRO-POL-ENV PROTEIN.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.
OX NCBI_TaxID=9606;
RN 11
RP SEQUENCE FROM N.A.
RA MEDLINE-99400989; PubMed-10469592;
RA Barbulescu M., Turner G., Seaman M.I., Delnard A.S., Kidd K.K.,
RA Lenz J.;
RT "Many human endogenous retrovirus K (HERV-K) proviruses are unique to
RT humans."
RL Curr. Biol. 9:861-868(1999).
CC -1- SIMILARITY: TO RNA-DIRECTED DNA POLYMERASE (REVERSE
CC TRANSCRIPTASE).
CC -1- SIMILARITY: BELONGS TO 2N-FINGER CCHC TYPE FAMILY.
CC -1- SIMILARITY: THE PROTEASE BELONGS TO THE PEPTIDASE FAMILY A1; ALSO
CC KNOWN AS THE EUKARYOTIC ASPARTYL PROTEASES FAMILY.

GenCore version 4.5
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OM protein - protein search, using sw model

Run on: April 9, 2002, 16:54:06; Search time 39.41 Seconds
(without alignments)
295.730 Million cell updates/sec

Title: US-09-490-700-36

Perfect score: 840

Sequence: 1 MVTPTWMDNPIEVYVND...ECVANSVILLQNEFTIID 153

Scoring table: BLOSUM62
Gapop 10.0, Gapext 0.5

Searched: 219241 seqs, 76174552 residues

Total number of hits satisfying chosen parameters: 219241

Minimum DB seq length: 0
Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%
Maximum Match 100%

Listing first 45 summaries

Database:

PIR_68:*
1: PIR1:*
2: PIR2:*
3: PIR3:*
4: PIR4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	768.5	91.5	584	4 VCHUER	retrovirus-related
2	82	9.8	226	2 A53273	MHC class II hist
3	81.5	9.7	990	2 T02309	probable transcrip
4	76	9.0	492	2 T26502	hypothetical prote
5	76	9.0	514	2 T26501	hypothetical prote
6	76	9.0	896	1 A35782	cytokine receptor
7	75.5	9.0	318	2 S76295	hypothetical prote
8	74.5	8.9	602	2 S39782	cyclooxygenase 1 -
9	74	8.8	466	2 A36724	transcription fact
10	73.5	8.8	297	2 T36724	probable membrane
11	73	8.7	1072	2 S76888	hypothetical prote
12	72.5	8.6	365	2 C86647	hypothetical prote
13	72.5	8.6	602	2 S69198	prostaglandin G/H
14	72.5	8.6	1475	2 A44765	alpha-amyrase (EC
15	72	8.6	341	2 T45350	hypothetical prote
16	72	8.6	688	1 VCMVMA	env polypote
17	72	8.6	848	1 C65083	hypothetical prote
18	71.5	8.5	481	2 S04605	glycyltin G3 - soyb
19	71.5	8.5	484	2 S11003	spheroidin precurs
20	71.5	8.5	1003	1 PYVZAM	hypothetical prote
21	71.5	8.5	1190	2 S21977	hypothetical prote
22	71.5	8.5	1262	2 T25168	hypothetical prote
23	71	8.5	251	2 B83413	conserved hypotet
24	70.5	8.4	295	2 F83201	molubdate-binding
25	70.5	8.4	387	2 B55164	scnl prote
26	70	8.3	256	2 T51150	probable transmem
27	70	8.3	491	2 B86155	env polypote
28	70	8.3	688	2 S26388	malate synthase (E
29	69.5	8.3	555	1 SYHOMA	

30	69.5	8.3	623	2 H96766	unknown protein F2
31	69.5	8.3	1274	2 T16251	hypothetical prote
32	69.5	8.3	1481	2 S28669	amylopullulanase p
33	69	8.2	204	2 T02386	hypothetical prote
34	69	8.2	1520	2 T00273	hypothetical prote
35	68.5	8.2	549	2 H86024	cytoplasmic trehal
36	68.5	8.2	549	2 S47739	probable alphaalp
37	68	8.1	214	1 RCBSCA	regulatory protein
38	68	8.1	355	2 T29659	hypothetical prote
39	68	8.1	688	1 VCMVMA	env polypote
40	68	8.1	876	2 PC2219	polypeptide - hepa
41	68	8.1	1210	2 S35548	DNA-directed RNA p
42	67.5	8.0	170	2 B71510	probable methyltra
43	67.5	8.0	285	2 T29490	hypothetical prote
44	67.5	8.0	473	2 S70357	forkhead transcrip
45	67.5	8.0	479	2 T01922	hypothetical prote

ALIGNMENTS

```
RESULT 1
VCHUER
retrovirus-related env polypote pseudogene - human
C:Species: Homo sapiens (man)
C:Date: 28-Dec-1987 #sequence_revision 04-Jan-1996 #text_change 14-May-1999
C:Accession: E24483
R:Ono, M.; Yasunaga, T.; Miyata, T.; Ushikubo, H.
J. Virol. 60, 589-598, 1986
A:Title: Nucleotide sequence of human endogenous retrovirus genome related to the mou
A:Reference number: A93023; MUID:87036922
A:Accession: E24483
A>Status: conceptual translation of pseudogene
A:Molecule type: DNA
A:Residues: 1-584 <ONO>
A:Cross-references: GB:M14123; NID:g182227
C:Genetics:
A:Gene: env
C:Keywords: capsid protein; coat protein; polypote; pseudogene

Query Match 91.5%; Score 768.5; DB 4; Length 584;
Best Local Similarity 94.7%; Pred. No. 4,7e-69;
Matches 142; Conservative 1; Mismatches 6; Indels 1; Gaps 1;

OY 4 PYTWMNDPIEVYVND...SVNPEPTDRCPAKPEEGMMINISIGYHPICIGRAPGLMP 63
      |||||
Db 1 PVTWMDNPIEVYVND...SVNPGPIDRCPAKPEEGMMINISIGYRPPICIGRAPGLMP 60
      |||||

OY 64 AVONMVLVEPTVSPNSRRTYHMVSGMSLRPRVNTLQDSYORSILKPRKGTCKREIPKG 123
      |||||
Db 61 AVONMVLVEPTVSPNSRRTYHMVSGMSLRPRVNTLQDSYORSILKPRKGTCKREIPKE 120
      |||||

OY 124 SKNTEVLMECVANSVILLQNEFTIID 153
      |||||
Db 121 SKNTEVLMECVANSVILLQNEFTIID 149
      |||||

RESULT 2
A53273
MHC class II histocompatibility antigen DR alpha chain - horse (fragment)
C:Species: Equus caballus (domestic horse)
C:Date: 12-May-1994 #sequence_revision 12-May-1994 #text_change 21-Jan-2000
C:Accession: A53273
R:Albright, D.; Bailey, E.; Woodward, J.G.
Immunogenetics 34, 136-138, 1991
A:Title: Nucleotide sequence of a cDNA clone of the horse (Equus caballus) DRa gene.
A:Reference number: A53273; MUID:91331619
A:Accession: A53273
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-226 <ALB>
A:Cross-references: GB:M60100; NID:g164236; PIDN:AAA30956.1; PID:g164237
```